REMARKS

A Petition for a One Month Extension of Time is filed herewith along with a Notice of Appeal to provide additional time for the Examiner to consider this response and then to proceed with the appeal, if necessary.

Applicants acknowledge with appreciation the indication of allowable subject matter in claims 50 and 51. Applicants most respectfully submit that all of the claims in the application are clearly patentable over the references applied in the prior art rejections. Therefore, Applicants have not restricted the claims to the indicated allowable subject matter at the present time.

Claims 42, 43, 44, 46 and 50 have been amended to more particularly define the invention taking into consideration the outstanding rejection under 35 U.S.C. 112, second paragraph. It is believed that the amendments to the claims obviate the rejection of claims 42-52 under 35 U.S.C. 112, second paragraph, by providing the antecedent basis in the claims requested in the Official Action. Applicants believe that this basis was already present in the rejected claims. The amendments to the claims are for clarification and to avoid the rejection under 35 U.S.C. 112, second paragraph. For example, the substance to be crystallised has been specified as lactose or lactose monohydrate as requested in the Official Action. Lactose and lactose monohydrate are defined in the preamble of the claim. Similarly, the antecedent basis of medium has been specified. These amendments do not raise new issues, are fully support by the specification. Entry of the Amendment is in order and is most respectfully requested.

The rejection of claims 42-49 and 52 under 35 U.S.C. 103 as being unpatentable over Hirao et al. in view of Trofast et al. has been carefully considered but is most respectfully traversed.

It is urged in the Official Action that Hirao teaches a process of shaping crystals of sugar alcohols by obtaining a saccharified starch solution with high maltose content, allowing crystallization, and separating the crystallized solid (column 2, lines 38 through column 3, lines 1-11). The viscosity of the solution can be regulated by the addition of

water-soluble organic solvent, or elevated temperature (column 4, lines 45-68; and example 1). However, there does not appear to be a disclosure of this in the cited column and lines or an explanation of the cited portion which would lead one of ordinary skill in the art to arrive at this teaching which is specifically traversed.

It is however, recognized in the Official Action that Hirao does not teach the viscosity of less than 25 Pas at a shear rate of $1s^{-1}$. It has been argued that this is a claim limitation which cannot be ignored and must be suggested in the prior art. This limitation is improperly ignored in the Official Action which states that, "However, no criticality is seen in the particular viscosity since Hirao obtains the same result desired by the applicant, e.g., a crystalline composition that is non-hydroscopic, free flowing, and can be in any desire size and shape (column 7, lines 33-53)". Accordingly, it is the position of the examiner that it would have been obvious for one of ordinary skill in the art to, by routine experimentation determine a suitable viscosity of the solution to obtain the claimed invention.

It is recognized in the Official Action that Hirao does not teach that the solid crystals can be used for inhalation. However, Hirao in column 5, lines 20-58 teaches besides anhydrous crystals of maltitol, other sugar alcohols such as sorbitol, maltotriitol and maltotetraitol can be used for various uses, e.g., for foods, cosmetics, and drugs. Hirao further teaches that maltitol or crystalline mixture solid can be prepared into desirable shape, including granule with a granulizer (column 7, lines 66 through column 8, lines 1-4). This statement is traversed since Hirao clearly states at column 8, line 1, that the admixture is then prepared into desirable shape. There is no suggestion of the elongation ratio required by claim 52. In an effort to overcome the deficiencies of the Hirao reference, the Trofast reference is cited.

It is urged in the Official Action that Trofast teaches a stable crystallinic form of fine-grained substance or substance mixture useful for inhalation (page 4, lines 23-30). The substance includes salbutamol sulfate, ipratropium bromide, or salmeterol xinafoate (page 7, lines 26 through page 8, lines 1-3). The substance may be combined with carriers suitable for inhalation, such as lactose, maltose, maltitol, starch, and its

hydrates (page 6, lines 21-31). Thus, it is concluded in the Official Action that it would have been obvious for one of ordinary skill in the art to optimize the solid crystalline mixture of Hirao as a carrier useful for inhalation of a pharmaceutical formulation in view of the teachings of Trofast, because the references teach the advantageous result in the use of carrier, such as maltitol and lactose monohydrate as a carrier for inhalation formulation. This rejection having been carefully considered but is most respectfully traversed.

Clearly, the rejection does not establish a prima facie case of obviousness of the claimed subject matter. The basis of the rejection is Hirao combined with Trofast and the assertion that all features not found in this combination of references namely, process steps b) and d) are of no criticality to the invention. Claims 28 and 32 are rejected to in light of all of the above plus Douglas. However, these claims are no longer present in the application. Clarification of any rejection of these claims is necessary for a meaningful response.

In any case, the Examiner's attention is also directed to MPEP section 2143.03 which states that all claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Applicants maintain the position that the rejected claims represent patentable subject matter and that the Examiner's rejections are merely based upon a hindsight mosaicing of two or three documents (along with conveniently ignoring all other features that cannot be found in these documents but which are claimed limitations). In re Fritch, 23 USPQ 1780, 1784(Fed Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.).

Applicants wish to point out that Hirao et al. is directed toward a very specific problem, i.e. a method for producing anhydrous crystals of maltitol. There is nothing in the teaching of this document to suggest to the skilled person that this methodology

would be applicable to lactose or lactose monohydrate in accordance with the presently claimed invention.

It is also urged in the Official Action that Trofast teaches a stable crystallinic form of fine-grained substance or substance mixture useful for inhalation. The substance includes salbutamol sulfate, ipratropium bromide, or salmeterol xinafoate. Various carriers may be mixed with the substance and conditioned. Again, this combination of references does not suggest the presently claimed invention, absent Applicants' teaching which may not be used as a teaching reference. It is further stated that it would have been obvious for one of ordinary skill in the art to optimize the solid crystalline mixture of Hirao as a carrier useful for inhalation of pharmaceutical formulation in view of the teachings of Trofast. However, such a combination does not result in the presently claimed invention as it would result in a maltitol containing composition.

It is recognized in the Official Action that Hirao does not teach a viscosity of less than 25 Pa.s at a shear rate of $1s^{-1}$. It is further urged that no criticality is seen in the particular viscosity since the prior art obtains the same result desired by Applicants, e.g. a crystalline composition that is non-hygroscopic, free-flowing and can be any desired size and shape. It is then concluded that it would have been prima facie obvious for one of ordinary skill in the art by routine experimentation to determine a suitable viscosity of the solution to obtain the claimed invention. These statements are specifically traversed.

Applicants most respectfully submit that the fact that a crystalline composition is obtained does not alter the fact that the obviousness of the claimed subject matter must be considered in light of the claim limitations which include the viscosity range as set forth in the claims. There must be motivation in the prior art to make the necessary changes to the process and Applicants' specification may not be used as a teaching reference. Absent the suggestion in the prior art with respect to the viscosity range and steps specified in the rejected claims, there is no expectation of success and therefore the rejection should be withdrawn.

The rejection of claims 28 and 32 under 35 U.S.C. 103(a) as being unpatentable over Hirao et al. in view of Trofast et al., and Douglas et al. has been carefully considered but it is noted that claims 28 and 32 are no longer pending in this application and therefore the rejection is moot.

Applicants in any case wish to note that Hirao and Trofast are relied upon for the reasons stated above. The references are silent as to the teaching of carbomer as a starch or binder in an aqueous solution. However, carbomer is a well known starch or thickener, or binder in pharmaceutical art. Douglas teaches an oral administration composition comprising starch or carbopol as an aqueous solution thickener (column 7, lines 22-32). Hence, it would have bene obvious for one of ordinary skill in the art to modify Hirao's starch solution using carbopol taught by Douglas. The unexpected result is free flowing crystal having desire size and shape.

Douglas et al. does not teach the use of an aqueous solution of Carbomer as being a medium suitable for use in a crystallization process for lactose and lactose monohydrate in accordance with the presently claimed invention. The equivalence of starch and carbomers is not used in the same context as that of the present invention.

Applicants also most respectfully direct the Examiner's attention to MPEP § 2144.08 (page 2100-114) wherein it is stated that Office personnel should consider all rebuttal argument and evidence present by applicant and the citation of In re Soni for error in not considering evidence presented in the specification.

Applicants wish to note that crystals prepared according to the presently claimed invention have significantly higher mean elongation ratio and surface smoothness as discussed on page 10 of the present specification. See also page 11 of Applicants' specification. Moreover, data within this specification at page 28 demonstrates that increasing the surface smoothness and elongation ratio gives rise to an increase in the fine particle fraction (FPF) of the drug delivered. Hirao et al is silent as to these crystalline properties which are not suggested by the prior art. A skilled person would not be motivated to use in Hirao et al process in the expectation of producing crystals

improved with these inhalation properties. Douglas et al. does not teach the use of an aqueous solution of carbomer as being a medium suitable for use in a crystallization process. The equivalence of starch and carbomers is not used in the same context as that of the present invention. Thus all of the claims in the application are patentable over. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 39-41 are rejected under 35 U.S.C. 103 as being unpatentable over Hirao et al., in view of Staniforth has been carefully considered but since these claims are no longer in the application, the rejection is moot.

In the Official Action it is urged that Hirao is relied upon for the reasons stated above. Hirao does not teach the size range of the crystallized solid.

It is stated that Staniforth teaches carrier particles useful in dry powder inhalers comprising one or more crystalline sugars including lactose, having particles diameter between from 60 μm to 180 μm (page 10, lines 2-17). Thus, it would have been obvious for one of ordinary skill in the art to modify Hirao crystalline solid carrier to have the particle size suitable for inhalation in view of the teachings of Staniforth, because the references teach the advantageous result in the use of crystalline sugars in pharmaceutical art. The unexpected result is a crystalline composition that is non-hygroscopic, free flowing, and can be in any desired size and shape. This conclusion is most respectfully traversed for the reasons already of record.

In the response to Applicants' previous amendment, it is urged in the Official Action that it is alleges that the crystal prepared according to the presently claimed invention have significantly higher mean elongation ratio and surface smoothness as discussed on page 10 of the present specification. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., significantly higher mean elongation ratio and surface smoothness) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations form the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Clearly, the corollary is this is that limitations in the claims may not be read out of the

claims. The process limitations for the process cannot be ignored and are not suggested by the prior art.

In view of the above comments and further amendments to the claims, favorable reconsideration and allowance of all of the claims now present in the application are most respectfully requested.

Respectfully submitted,

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